WEST Search History

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updated search 4/05 RP

DATE: Thursday, April 28, 2005

Hide?	Set Name	Query	Hit Count
		DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=AND	
☐	L1	holmes.in. and (holotoxin$ or holo-toxin$ or ab-5 or ab5 or adpribosylating or adp-ribosylat$ or rtx or rtxs)	59
		DB=USPT; PLUR=YES; OP=AND	
☐	L2	l1 and cholera	24
		DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=AND	
☐	L3	l1 and cholera	47
☐	L4	L3 not l2	23
		DB=PGPB; PLUR=YES; OP=AND	
☐	L5	US-20040176571-A1.did.	1
		DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=AND	
☐	L6	(jobling or eldridge or hancock or peek).in.	5209
☐	L7	l6 and cholera	25
☐	L8	L7 not l4 not l2	18
☐	L9	L7 not l4 not l2	18
☐	L10	(holotoxin$ or holo-toxin$ or ab-5 or ab5 or adpribosylating or adp-ribosylat$ or rtx or rtxs).clm.	133
☐	L11	L10 and (changes or changed or modified or mutant or mutation or mutagenesis or alter or altered or modification or substitution or deletion or insertion).clm.	76
☐	L12	L11 and (glutamic or aspartic).clm.	6
☐	L13	L11 and (glutamine or aspartic).clm.	7

END OF SEARCH HISTORY

1. 20040197348. 20 Feb 04. 07 Oct 04. Enhanced immune response to attachment (G) protein of respiratory Syncytial virus. Hancock, Gerald E., et al. 424/186.1; 530/350 C07K014/005 C12Q001/70 A61K039/12.

☐ 2. 20040057948. 03 Jun 03. 25 Mar 04. Component of bromelain. Mynott, Tracey Lehanne, et al. 424/94.65; 435/212 A61K038/46 C12N009/48.

☐ 3. 20020188107. 28 Dec 01. 12 Dec 02. Component of stem bromelain. Mynott, Tracey Lehanne, et al. 530/379; 435/219 530/300 530/350 530/370 530/412 536/23.72 C12N009/50 C07H021/04 C07K002/00 C07K004/00 C07K005/00 C07K007/00 C07K014/00 C07K016/00 C07K017/00 A61K038/00 C07K001/00 A61K035/78 A61K035/80 A23J001/00.

☐ 4. 20020102253. 29 Dec 00. 01 Aug 02. Component of bromelain. Mynott, Tracey Lehanne, et al. 424/94.65; 435/219 A61K038/46 C12N009/50.

☐ 5. 6699478. 15 Mar 00; 02 Mar 04. Enhanced immune response to attachment (G) protein of Respiratory Syncytial Virus. Hancock; Gerald E., et al. 424/211.1; 424/186.1 424/202.1 424/204.1 435/235.1 530/300 530/350. A61K039/155 A61K039/295 A61K039/12 C12N007/01 C07K007/00 C07K017/00.

☐ 6. 6335427. 25 Aug 99; 01 Jan 02. Component of stem bromelain. Mynott; Tracey Lehanne, et al. 530/379; 530/350 530/370 530/412. A61K035/78.

☐ 7. 6309851. 19 Mar 98; 30 Oct 01. Method for producing a recombinant protein. Taylor; Ronald K., et al. 435/25; 435/69.1. C12Q001/26.

☐ 8. 6024983. 07 Sep 93; 15 Feb 00. Composition for delivering bioactive agents for immune response and its preparation. Tice; Thomas R., et al. 424/501; 424/237.1 424/256.1 424/497 424/499 424/810 428/402.21 428/402.24 514/885 514/889 514/958 514/963. A61K009/52 A61K039/085 A61K039/12 A61K039/39.

☐ 9. 5942252. 06 Jun 95; 24 Aug 99. Method for delivering bioactive agents into and through the mucosally-associated lymphoid tissues and controlling their release. Tice; Thomas R., et al. 424/501; 424/426 424/430 424/434 424/435 424/436 424/451 424/464. A61K009/50 A61K009/48 A61F002/02 A61F009/02.

☐ 10. 5853763. 06 Jun 95; 29 Dec 98. Method for delivering bioactive agents into and through the mucosally-associated lymphoid tissue and controlling their release. Tice; Thomas R., et al. 424/489; 424/184.1 424/204.1 424/206.1 424/234.1 424/237.1 424/434 424/435 424/436 424/499 424/501 424/810 514/885 514/888 514/963. A61K009/52 A61K039/085 A61K039/12 A61K039/39.

☐ 11. 5820883. 06 Jun 95; 13 Oct 98. Method for delivering bioactive agents into and through the mucosally-associated lymphoid tissues and controlling their release. Tice; Thomas R., et al. 424/501; 424/237.1 424/256.1 424/497 424/810 514/885 514/888 514/963. A61K009/52 A61K039/085 A61K039/12 A61K039/39.

☐ 12. 5814344. 06 Jun 95; 29 Sep 98. Method for delivering bioactive agents into and through the mucosally associated lymphoid tissues and controlling their release. Tice; Thomas R., et al. 424/501; 424/237.1 424/256.1 424/497 424/810 514/885 514/888 514/963. A61K009/52 A61K039/085 A61K039/12 A61K039/39.

☐ 13. 5811128. 07 Sep 93; 22 Sep 98. Method for oral or rectal delivery of microencapsulated vaccines and compositions therefor. Tice; Thomas R., et al. 424/501; 424/237.1 424/256.1 424/497 424/810 428/402.21 428/402.24 514/885 514/888 514/963. A61K009/52 A61K039/085 A61K039/12 A61K039/39.

☐ 14. 5786166. 17 Jan 95; 28 Jul 98. Methods for determining effects of a compound on the activity of bacterial periplasmic oxidoreductase enzymes. Taylor; Ronald K., et al. 435/25; 435/184 435/32. C12Q001/26 C12Q001/18 C12N009/99.

☐ 15. 5382660. 25 Oct 91; 17 Jan 95. TcpG gene of vibrio cholerae. Taylor; Ronald K., et al. 536/23.2; 536/23.1 536/23.7. C12N015/31 C12N015/52.

☐ 16. 4937182. 07 Feb 89; 26 Jun 90. Method for predicting chemosensitivity of anti-cancer drugs. Hancock; Miriam E. C., et al. 435/29;. C12Q001/02.

☐ 17. 4816395. 19 Dec 85; 28 Mar 89. Method for predicting chemosensitivity of anti-cancer drugs. Hancock; Miriam E. C., et al. 435/29; 436/800 436/813. C12Q001/02.

☐ 18. US 5382660A. New TcpG gene from Vibrio cholerae - used for insertion to bacterial genetic material to increase the prodn of non-bacterial or bacterial proteins.. PEEK, J A, et al. C12N015/31 C12N015/52.

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US-PAT-NO: 6309851
DOCUMENT-IDENTIFIER: US 6309851 B1

TITLE: Method for producing a recombinant protein

DATE-ISSUED: October 30, 2001

INT-CL: [07] C12 Q 1/26

US-CL-ISSUED: 435/25; 435/69.1
US-CL-CURRENT: 435/25; 435/69.1

FIELD-OF-SEARCH: 435/172.1, 435/243, 435/252.1, 435/252.3, 435/69.1

1. Document ID: US 20040176571 A1

L5: Entry 1 of 1 File: PGPB Sep 9, 2004

PGPUB-DOCUMENT-NUMBER: 20040176571
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040176571 A1

TITLE: Mutant forms of cholera holotoxin as an adjuvant

PUBLICATION-DATE: September 9, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Green, Bruce A.	Pittsford	NY	US	
Holmes, Randall K.	Golden	CO	US	
Jobling, Michael G.	Aurora	CO	US	
Zhu, Duzhang	Rochester	NY	US	

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	COUNTRY	TYPE CODE
Wyeth Holdings Corporation	Madison	NJ	US	02

APPL-NO: 10/ 478308 [PALM]
DATE FILED: December 4, 2003

RELATED-US-APPL-DATA:
Application is a non-provisional-of-provisional application 60/296531, filed June 7, 2001,

PCT-DATA:

DATE-FILED	APPL-NO	PUB-NO	PUB-DATE	371-DATE	102(E)-DATE
Jun 5, 2002	PCT/US02/21008				

INT-CL: [07] A61 K 39/106, C07 K 1/00, C07 K 14/00, C07 K 17/00

US-CL-PUBLISHED: 530/350
US-CL-CURRENT: 530/350

ABSTRACT:

Mutant cholera holotoxins having single or double amino acid substitutions or insertions have reduced toxicity compared to the wild-type cholera holotoxin. The mutant cholera holotoxins are useful as adjuvants in antigenic compositions to enhance the immune response in a vertebrate host to a selected antigen from a pathogenic bacterium, virus, fungus, or parasite, a cancer cell, a tumor cell, an allergen, or a self-molecule.

CROSS-REFERENCE TO OTHER APPLICATIONS

[0001] This application claims the benefit of the priority of U.S. provisional patent application No. 60/296,531, filed Jun. 7, 2001.

Entry 6 of 7 File: USPT Jul 20, 1999

US-PAT-NO: 5925546
DOCUMENT-IDENTIFIER: US 5925546 A

TITLE: Immunologically active polypeptides with altered toxicity useful for the preparation of an antipertussis vaccine

DATE-ISSUED: July 20, 1999

INT-CL: [06] C12 P 21/02, C12 N 15/00

US-CL-ISSUED: 435/69.3; 435/320.1, 536/23.7, 424/190.1, 424/254.1, 424/832
US-CL-CURRENT: 435/69.3; 424/190.1, 424/254.1, 424/832, 435/320.1, 536/23.7

FIELD-OF-SEARCH: 530/350, 424/240.1, 424/190.1, 424/254.1, 424/832, 435/69.1, 435/69.3, 435/172.3, 435/320.1, 536/23.7

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L4: Entry 19 of 23 File: EPAB Dec 12, 2002

PUB-NO: WO002098369A2
DOCUMENT-IDENTIFIER: WO 2098369 A2
TITLE: MUTANT FORMS OF CHOLERA HOLOTOXIN AS AN ADJUVANT

PUBN-DATE: December 12, 2002

INVENTOR-INFORMATION:

NAME	COUNTRY
GREEN, BRUCE A	US
HOLMES, RANDALL K	US
JOBLING, MICHAEL G	US
ZHU, DUZHANG	US

ASSIGNEE-INFORMATION:

NAME	COUNTRY
AMERICAN CYANAMID CO	US
GOVERNMENT OF THE US UNIFORMED	US
GREEN BRUCE A	US
HOLMES RANDALL K	US
JOBLING MICHAEL G	US
ZHU DUZHANG	US

APPL-NO: US00221008
APPL-DATE: June 5, 2002

PRIORITY-DATA: US29653101P (June 7, 2001)

INT-CL (IPC): A61 K 0/
EUR-CL (EPC): A61K039/39; C07K014/28

ABSTRACT:

CHG DATE=20030204 STATUS=O>Mutant cholera holotoxins having single or double amino acid substitutions or insertions have reduced toxicity compared to the wild-type cholera holotoxin. The mutant cholera holotoxins are useful as adjuvants in antigenic compositions to enhance the immune response in a vertebrate host to a selected antigen from a pathogenic bacterium, virus, fungus, or parasite, a cancer cell, a tumor cell, an allergen, or a self-molecule.

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PUB-NO: WO002098368A2
DOCUMENT-IDENTIFIER: WO 2098368 A2
TITLE: MUTANT FORMS OF CHOLERA HOLOTOXIN AS AN ADJUVANT

PUBN-DATE: December 12, 2002

INVENTOR-INFORMATION:

NAME	COUNTRY
GREEN, BRUCE A	US
HOLMES, RANDALL K	US
JOBLING, MICHAEL G	US
ZHU, DUZHANG	US

ASSIGNEE-INFORMATION:

NAME	COUNTRY
AMERICAN CYANAMID CO	US
UNIV COLORADO	US
GREEN BRUCE A	US
HOLMES RANDALL K	US
JOBLING MICHAEL G	US
ZHU DUZHANG	US

APPL-NO: US00220978
APPL-DATE: June 5, 2002

PRIORITY-DATA: US29653701P (June 7, 2001)

INT-CL (IPC): A61 K 0/
EUR-CL (EPC): A61K039/39; C07K014/28

ABSTRACT:

CHG DATE=20030204 STATUS=O>Mutant cholera holotoxins comprising a cholera toxin subunit (A) having single amino acid substitutions in the amino acid positions (16 or 72) or a double amino acid positions (16 and 68) or (68 and 72) have reduced toxicity compared to the wild-type cholera holotoxin. The mutant cholera holotoxins are useful as adjuvants in immunogenic compositions to enhance the immune response in a vertebrate host to a selected antigen from a pathogenic bacterium, virus, fungus, or parasite, a cancer cell, a tumor cell, an allergen, or a self-molecule.

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Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. De

Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

Terms	Documents
US-20040176571-A1.did.	1

DOCUMENT-IDENTIFIER: US 20040197348 A1
TITLE: Enhanced immune response to attachment (G) protein of respiratory Syncytial virus

INVENTOR:
Hancock, Gerald E.

Detail Description Paragraph:
[0064] Suitable adjuvants include vegetable oils or emulsions thereof, surface active substances, e.g., hexadecylamin, octadecyl amino acid esters, octadecylamine, lysolecithin, dimethyl-dioctadecylammonium bromide, N,N-dicoctadecyl-N'-N'bis(2-hydroxyethyl-propane diamine), methoxyhexadecylglycerol, and pluronic polyols; polyamines,e.g., pyran, dextransulfate, poly IC, carbopol; peptides, e.g., muramyl dipeptide, dimethylglycine, tuftsin; immune stimulating complexes; oil emulsions; mineral gels; aluminum compounds such as aluminum hydroxide and aluminum phosphate; MPL.TM. (3-O-deacylated monophosphoryl lipid A, RIBI ImmunoChem Research, Inc., Hamilton, Mont.); detoxified mutants of Cholera toxin and E. coli heat labile toxin; naked DNA CpG motifs; and Stimulon.TM. QS-21 (Aquila Biopharmaceuticals, Inc., Framingham, Mass.). The altered G protein or polypeptide of this invention can also be incorporated into liposomes or ISCOMS (immunostimulating complexes), and supplementary active ingredients may also be employed. The antigens of the present invention can also be administered in combination with lymphokines, including, but not limited to, IL-2, IL-3, IL-12, IL-15, IFN-.gamma. and GM-CSF.

DOCUMENT-IDENTIFIER: US 6309851 B1
TITLE: Method for producing a recombinant protein

INVENTOR (2):
Peek; Joel A.

Brief Summary Text (8):
The parent application teaches that preventing a microorganism from producing its oxidoreductase enzyme results in the production of inactive virulence determinants due to the lack of active 3-dimensional conformation. The parent application presents data showing that the lack of the periplasmic oxidoreductase enzyme TcpG in mutant Vibrio cholerae is responsible for failure of the mutants to produce active virulent cholera toxin.

Drawing Description Text (5):
FIG. 4 is a western blot showing a comparison of 0395, JP100 and KP8-96 cholera toxins.

DOCUMENT-IDENTIFIER: US 5820883 A
TITLE: Method for delivering bioactive agents into and through the mucosally-associated lymphoid tissues and controlling their release

INVENTOR (3):
Eldridge; John H.

Detailed Description Text (125):
In both man and animals, it has been shown that systemic immunization coupled with mucosal presentation of antigen is more effective than any other combination in promoting mucosal immune responses (Pierce, N. F. and Gowans, J. L. Cellular kinetics of the intestinal immune response to cholera toxoid in rats. J. Exp. Med. 142:1550; 1975). Three groups of mice were primed by IP immunization with 100 micrograms of microencapsulated SEB toxoid and 30 days later were challenged with 100 micrograms of microencapsulated SEB toxoid by either the IP, oral or IT routes. This was done to directly determine if a mixed immunization protocol utilizing microencapsulated antigen was advantageous with respect to the levels of sIgA induced.

First Hit Fwd Refs

L8: Entry 15 of 18 File: USPT Jan 17, 1995

DOCUMENT-IDENTIFIER: US 5382660 A
TITLE: TcpG gene of vibrio cholerae

INVENTOR (2):
Peek; Joel A.

Detailed Description Text (13):
J. Altered cholera toxin subunit profile in KP8-96. Homology to thiol:sulfide interchange proteins led us to investigate whether other disulfide bond containing ToxR regulated virulence factors were affected by a mutation in TcpG. The A subunit of cholera toxin contains a disulfide bond. To assess the effects of TcpG on toxin, cultures of KP8-96 and 0395 were grown to an equivalent optical density at 600 nm under toxin expressing conditions. Both whole cell and supernatant samples were resolved by SDS-PAGE and analyzed by Western blot using a polyclonal anti-holotoxin antibodies or anti-toxin A subunit antibodies. There are several differences that are notable between the two strains. More toxin B subunit is present in the monomeric form in KP8-96 than in the wild type strain. This corresponds to a reduced pentamerization of the B subunit in the mutant strain. Most interestingly, the toxin A subunit profiles are markedly different between the two strains. The A subunit of 0395 was found in the unnicked A form in the whole cell extracts, and both the unnicked A and A1 forms in the culture supernatant. KP8-96, on the other hand, showed elevated levels of unnicked A and virtually no A1 form in the culture supernatant. Thus, the A1 form was lunable to migrate out of the bacterium due to the lack of the TcpG enzyme. The wild type 0395, however, with an intact TcpG gene sequence, was able to secrete both A and A1. This result suggests that the TcpG-PhoA fusion causes a greatly decreased ability of the A subunit to associate with the B subunit in an export competent form. A similar result is seen with a tcpG knockout mutation that does not produce a hybrid TcpG protein that could possibly interfere with the extracellular secretion process.

Other Reference Publication (3):
D. M. Gill, "Mechanism of Action of Cholera Toxin", in Advances in Cyclic Nucleotide Research, ed. P. Greegard, et al., Raven Press, New York, pp. 85-118 (1977).

Other Reference Publication (9):
R. K. Taylor, et al., "Use of phoA Gene Fusions to Identify a Pilus Colonization Factor Coordinately Regulated With Cholera Toxin", Proc. Natl. Acad. Sci. USA, vol. 84, pp. 2833-2837 (1987).

DOCUMENT-IDENTIFIER: US 5925546 A
TITLE: Immunologically active polypeptides with altered toxicity useful for the preparation of an antipertussis vaccine

CLAIMS:

1. A method for the preparation of an immunologically active mutant polypeptide having no or reduced toxicity, which method comprises:

(a) modifying by site-directed mutagensis the DNA of the S1 subunit of the gene in the operon which codes for pertussis toxin by substitution in one or more sites of said S1 subunit the DNA sequence coding for a substitute amino acid for the DNA coding for an amino acid at said site in said S1 subunit:

(b) constructing a hybrid plasmid linking a cloning vector with said DNA of said S1 subunit;

(c) transforming a host microorganism with said hybrid plasmid;

(d) cultivating said transformed microorganism in a suitable culture medium; and

(e) recovering said mutant polypeptide produced by said microorganism;

said substitution comprising said substitute amino acids being selected from the group consisting of:

(1) glutamic acid at position 129 substituted by glycine at position 129;

(2) tyrosine at position 8 and arginine at position 9 substituted by aspartic acid at position 8 and glycine at position 9; and

(3) phenylalanine at position 50 and threonine at position 53 substituted by glutamic acid at position 50 and isolucine at position 53.

3. The method of claim 1 wherein wherein said substitute amino acids comprise tyrosine at position 8 and arginine at position 9 substituted by aspartic acid at position 8 and glycine at position 9.

5. The method of claim 1 wherein said mutant polypeptide exhibits a complete loss of ADP-ribosylation activity as compared with natural pertussis toxin.

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20040181036. 04 Dec 03. 16 Sep 04. Mutant forms of cholera holotoxin as an adjuvant. Green, Bruce A, et al. 530/350; A61K039/106 C07K001/00 C07K014/00 C07K017/00.

☐ 2. 20040176571. 04 Dec 03. 09 Sep 04. Mutant forms of cholera holotoxin as an adjuvant. Green, Bruce A., et al. 530/350; A61K039/106 C07K001/00 C07K014/00 C07K017/00.

☐ 3. WO 200298369A. Novel immunogenic, mutant cholera holotoxin useful for enhancing immune response of vertebrate host to antigen, comprises amino sequence of subunit A of wild-type cholera toxin. GREEN, B A, et al. A61K000/00 A61K006/00 A61K039/00 A61K039/002 A61K039/008 A61K039/015 A61K039/02 A61K039/04 A61K039/05 A61K039/07 A61K039/08 A61K039/085 A61K039/09 A61K039/095 A61K039/10 A61K039/102 A61K039/106 A61K039/108 A61K039/112 A61K039/118 A61K039/12 A61K039/125 A61K039/13 A61K039/145 A61K039/15 A61K039/155 A61K039/165 A61K039/175 A61K039/20 A61K039/205 A61K039/21 A61K039/215 A61K039/23 A61K039/235 A61K039/245 A61K039/255 A61K039/265 A61K039/29 A61K039/35 A61K039/39 A61K039/42 C07K001/00 C07K014/00 C07K014/28 C07K017/00 C12N001/15 C12N001/19 C12N001/21 C12N005/10 C12N015/09 C12P021/02.

☐ 4. WO 200298368A. Novel immunogenic mutant cholera holotoxin for preparing immunogenic composition for enhancing immune response of vertebrate host to bacterial or viral antigen, has reduced toxicity compared to wild-type cholera toxin. GREEN, B A, et al. A61K000/00 A61K039/00 A61K039/002 A61K039/008 A61K039/02 A61K039/095 A61K039/102 A61K039/106 A61K039/12 A61K039/245 A61K039/35 A61K039/39 A61K039/42 C07K001/00 C07K014/00 C07K014/28 C07K017/00 C12N001/15 C12N001/19 C12N001/21 C12N005/10 C12N015/09 C12P021/02.

☐ 5. WO 200018434A. New mutant cholera holotoxin having a point mutation at amino acid position 29 of the A subunit useful as an adjuvant in an antigenic composition to enhance the immune response in a vertebrate host to a selected antigen from a pathogen. ELDRIDGE, J H, et al. A61K039/00 A61K039/002 A61K039/02 A61K039/095 A61K039/102 A61K039/106 A61K039/12 A61K039/15 A61K039/155 A61K039/245 A61K039/39 A61P037/04 C07K014/14 C07K014/22 C07K014/28 C07K014/285 C07K014:28 C12N001/15 C12N001/19 C12N001/21 C12N005/10 C12N015/09 C12N015/63 C12P021/02.

☐ 6. 3192658. 06 Jul 65. Classified directory structure. MCGURN ROBERT S. 40/389;.

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Terms	Documents
ctcrm or ct-crm	6

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CLUSTAL W (1.74) multiple sequence alignment


sp|P01555|CHTA_VIBCH        MVKIIFVFFI---FLSSFSYANDDKLYRADSRPPDEIKQSGGLMPRGQSE
tr|Q8L356|Q8L356_VIBCH      MVKIIFVFFI---FLSSFSYANDDKLYRADSRPPDEIKQSGGLMPRGQSE
sp|P06717|ELAP_ECOLI        MKNITFIFFI---LLASPLYANGDRLYRADSRPPDEIKRSGGLMPRGHNE
tr|O66280|O66280_ECOLI      MKNITFIFFI---LLASPLYANGDKLYRADSRPPDEIKRSGGLMPRGHNE
sp|P43530|ELAH_ECOLI        MKNITFIFFI---LLASPLYANGDKLYRADSRPPDEIKRSGGLMPRGHNE
tr|Q6U8A2|Q6U8A2_VIBCH      ----------------------------RADSRPPDEIKQSGGLMPRGQSE
tr|Q6U8A3|Q6U8A3_VIBCH      ----------------------------WADSRPPDEIKQSGGLMPRGQSE
sp|P43528|E2BA_ECOLI        -MAKVISFFISLFLISFPLYAN--DYFRADSRTPDEVRRSGGLIPRGQDE
sp|P13810|E2AA_ECOLI        MIKHVLLFFV---FISFSVSAN--DFFRADSRTPDEIRRAGGLLPRGQQE
                                                    ****.***::::***:***:.*

sp|P01555|CHTA_VIBCH        YFDRGTQMNINLYDHARGTQTGFVRHDDGYVSTSISLRSAHLVGQTILSG
tr|Q8L356|Q8L356_VIBCH      YFDRGTQMNINLYDHARGTQTGFVRHDDGYVSTSISLRSAHLVGQTILSG
sp|P06717|ELAP_ECOLI        YFDRGTQMNINLYDHARGTQTGFVRYDDGYVSTSLSLRSAHLAGQSILSG
tr|O66280|O66280_ECOLI      YFDRGTQMNINLYDHARGTQTGFVRYDDGYVSTSLSLRSAHLAGQSILSG
sp|P43530|ELAH_ECOLI        YFDRGTQMNINLYDHARGTQTGFVRYDDGYVSTSLSLRSAHLAGQSILSG
tr|Q6U8A2|Q6U8A2_VIBCH      YFDRGTQMNINLYDHARGTQTGFVRHDDGYVSTSISLRSAHLVGQTILSG
tr|Q6U8A3|Q6U8A3_VIBCH      YFDRGTQMNINLYDHARGTQTGFVRHDDGYVSTSISLRSAHLVGQTILSG
sp|P43528|E2BA_ECOLI        AYERGTPININLYDHARGTATGNTRYNDGYVSTTTTLRQAHLLGQNMLGG
sp|P13810|E2AA_ECOLI        AYERGTPININLYEHARGTVTGNTRYNDGYVSTTVTLRQAHLIGQNILGS
                             ::*** :*****:***** ** .*::******: :**.*** **.:*..

sp|P01555|CHTA_VIBCH        HSTYYIYVIATAPNMFNVNDVLGAYSPHPDEQEVSALGGIPYSQIYGWYR
tr|Q8L356|Q8L356_VIBCH      HSTYYIYVIATAPNMFNVNDVLGAYSPHPDEQEVSALGGIPYSQIYGWYR
sp|P06717|ELAP_ECOLI        YSTYYIYVIATAPNMFNVNDVLGVYSPHPYEQEVSALGGIPYSQIYGWYR
tr|O66280|O66280_ECOLI      YSTYYIYVIATAPNMFNVNDVLGVYSPHPYEQEVSALGGIPYSQIYGWYR
sp|P43530|ELAH_ECOLI        YSTYYIYVIATAPNMFNVNDVLGVYSPHPYEQEVSALGGIPYSQIYGWYR
tr|Q6U8A2|Q6U8A2_VIBCH      HSTYYIYVIATAPNMFNVNDVLGAYSPHPDEQEVSALGGIPYSQIYGWYR
tr|Q6U8A3|Q6U8A3_VIBCH      HSTYYIYVIATAPNMFNVNDVLGAYSPHPDEQGVSALGGIPYSQIYGWYR
sp|P43528|E2BA_ECOLI        YNEYYIYVVAAAPNLFDVNGVLGRYSPYPSENEYAALGGIPLSQIIGWYR
sp|P13810|E2AA_ECOLI        YNEYYIYVVAPAPNLFDVNGVLGRYSPYPSENEFAALGGIPLSQIIGWYR
                            :. *****:*.***:*:**.*** ***:* *:  :****** *** ****

sp|P01555|CHTA_VIBCH        VHFGVLDEQLHRNRGYRDRYYSNLDIAPAADGYGLAGFPPEHRAWREEPW
tr|Q8L356|Q8L356_VIBCH      VHFGVLDEQLHRNRGYRDRYYSNLDIAPAADGYGLAGFPPEHRAWREEPW
sp|P06717|ELAP_ECOLI        VNFGVIDERLHRNREYRDRYYRNLNIAPAEDGYRLAGFPPDHQAWREEPW
tr|O66280|O66280_ECOLI      VNFGVIDERLHRNREYRDRYYRNLNIAPAEDGYRLAGFPPDHQAWREEPW
sp|P43530|ELAH_ECOLI        VNFGVIDERLHRNREYRDRYYRNLNIAPAEDGYRLAGFPPDHQAWREEPW
tr|Q6U8A2|Q6U8A2_VIBCH      VHFGVLDEQLHRNRGYRDRYYSNLDIAPAADGYGLAGFPPEHRAWREEPW
tr|Q6U8A3|Q6U8A3_VIBCH      VHFGVLDEQLHRNRGYRDRYYSNLDIAPAADGYGLAGFPPEHRAWREEPW
sp|P43528|E2BA_ECOLI        VSFGAIEGGMHRNRDYRRDLFRGLSAAPNEDGYRIAGFPDGFPAWEEVPW
sp|P13810|E2AA_ECOLI        VSFGAIEGGMQRNRDYRGDLFRGLTVAPNEDGYQLAGFPSNFPAWREMPW
                            * **.::  ::*** **   : .*  **  *** :****  . **.* **

sp|P01555|CHTA_VIBCH        IHHAPPGCGNAPRSSMSNTCDEKTQSLGVKFLDEYQSKVKRQIFSGYQSD
tr|Q8L356|Q8L356_VIBCH      IHHAPPGCGNAPRSSMSNTCDEKTQSLGVKFLDEYQSKVKRQIFSGYQSD
sp|P06717|ELAP_ECOLI        IHHAPQGCGNSSRTITGDTCNEETQNLSTIYLREYQSKVKRQIFSDYQSE
tr|O66280|O66280_ECOLI      IHHAPQGCGNSSRTITDDTCNEETQNLSTIYLRKYQSKVKRQIFSDYQSE
sp|P43530|ELAH_ECOLI        IHHAPQGCGNSSRTITGDTCNEETQNLSTIYLRKYQSKVKRQIFSDYQSE
tr|Q6U8A2|Q6U8A2_VIBCH      IHHAPPGCGNAPRSS-----------------------------------
tr|Q6U8A3|Q6U8A3_VIBCH      IHHAPPGCGNAPRSS-----------------------------------
sp|P43528|E2BA_ECOLI        REFAPNSCLPNNKASSDTTCASLTNKLSQHDLADFKKYIKRKFTLMTLLS
sp|P13810|E2AA_ECOLI        STFAPEQCVPNNKEFKGGVCISATNVLSKYDLMNFKKLLKRRLALTFFMS
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sp|P01555|CHTA_VIBCH        ID-----THNRIKDEL
tr|Q8L356|Q8L356_VIBCH      ID-----THNRIEDEL
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sp|P06717|ELAP_ECOLI        VD-----IYNRIRDEL
tr|O66280|O66280_ECOLI      VD-----IYNRIRDEL
sp|P43530|ELAH_ECOLI        VD-----IYNRIRNEL
tr|Q6U8A2|Q6U8A2_VIBCH      ----------------
tr|Q6U8A3|Q6U8A3_VIBCH      ----------------
sp|P43528|E2BA_ECOLI        INNDGFFSNNGGKDEL
sp|P13810|E2AA_ECOLI        E--DDFIGVHGERDEL
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PileUp

MSF: 266 Type: P Check: 944 ..

Name: sp|P01555|CHTA_VIBCH oo Len: 266 Check: 1990 Weight: 0.100
Name: tr|Q8L356|Q8L356_VIBCH oo Len: 266 Check: 1780 Weight: 0.100
Name: sp|P06717|ELAP_ECOLI oo Len: 266 Check: 3718 Weight: 0.100
Name: tr|O66280|O66280_ECOLI oo Len: 266 Check: 3441 Weight: 0.100
Name: sp|P43530|ELAH_ECOLI oo Len: 266 Check: 3939 Weight: 0.100
Name: tr|Q6U8A2|Q6U8A2_VIBCH oo Len: 266 Check: 3206 Weight: 0.100
Name: tr|Q6U8A3|Q6U8A3_VIBCH oo Len: 266 Check: 3384 Weight: 0.100
Name: sp|P43528|E2BA_ECOLI oo Len: 266 Check: 1062 Weight: 0.100
Name: sp|P13810|E2AA_ECOLI oo Len: 266 Check: 8424 Weight: 0.100

//

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sp|P01555|CHTA_VIBCH        MVKIIFVFFI ...FLSSFSY ANDDKLYRAD SRPPDEIKQS GGLMPRGQSE
tr|Q8L356|Q8L356_VIBCH      MVKIIFVFFI ...FLSSFSY ANDDKLYRAD SRPPDEIKQS GGLMPRGQSE
sp|P06717|ELAP_ECOLI        MKNITFIFFI ...LLASPLY ANGDRLYRAD SRPPDEIKRS GGLMPRGHNE
tr|O66280|O66280_ECOLI      MKNITFIFFI ...LLASPLY ANGDKLYRAD SRPPDEIKRS GGLMPRGHNE
sp|P43530|ELAH_ECOLI        MKNITFIFFI ...LLASPLY ANGDKLYRAD SRPPDEIKRS GGLMPRGHNE
tr|Q6U8A2|Q6U8A2_VIBCH      .......... .......... .......RAD SRPPDEIKQS GGLMPRGQSE
tr|Q6U8A3|Q6U8A3_VIBCH      .......... .......... .......WAD SRPPDEIKQS GGLMPRGQSE
sp|P43528|E2BA_ECOLI        .MAKVISFFI SLFLISFPLY AN..DYFRAD SRTPDEVRRS GGLIPRGQDE
sp|P13810|E2AA_ECOLI        MIKHVLLFFV ...FISFSVS AN..DFFRAD SRTPDEIRRA GGLLPRGQQE

sp|P01555|CHTA_VIBCH        YFDRGTQMNI NLYDHARGTQ TGFVRHDDGY VSTSISLRSA HLVGQTILSG
tr|Q8L356|Q8L356_VIBCH      YFDRGTQMNI NLYDHARGTQ TGFVRHDDGY VSTSISLRSA HLVGQTILSG
sp|P06717|ELAP_ECOLI        YFDRGTQMNI NLYDHARGTQ TGFVRYDDGY VSTSLSLRSA HLAGQSILSG
tr|O66280|O66280_ECOLI      YFDRGTQMNI NLYDHARGTQ TGFVRYDDGY VSTSLSLRSA HLAGQSILSG
sp|P43530|ELAH_ECOLI        YFDRGTQMNI NLYDHARGTQ TGFVRYDDGY VSTSLSLRSA HLAGQSILSG
tr|Q6U8A2|Q6U8A2_VIBCH      YFDRGTQMNI NLYDHARGTQ TGFVRHDDGY VSTSISLRSA HLVGQTILSG
tr|Q6U8A3|Q6U8A3_VIBCH      YFDRGTQMNI NLYDHARGTQ TGFVRHDDGY VSTSISLRSA HLVGQTILSG
sp|P43528|E2BA_ECOLI        AYERGTPINI NLYDHARGTA TGNTRYNDGY VSTTTTLRQA HLLGQNMLGG
sp|P13810|E2AA_ECOLI        AYERGTPINI NLYEHARGTV TGNTRYNDGY VSTTVTLRQA HLIGQNILGS

sp|P01555|CHTA_VIBCH        HSTYYIYVIA TAPNMFNVND VLGAYSPHPD EQEVSALGGI PYSQIYGWYR
tr|Q8L356|Q8L356_VIBCH      HSTYYIYVIA TAPNMFNVND VLGAYSPHPD EQEVSALGGI PYSQIYGWYR
sp|P06717|ELAP_ECOLI        YSTYYIYVIA TAPNMFNVND VLGVYSPHPY EQEVSALGGI PYSQIYGWYR
tr|O66280|O66280_ECOLI      YSTYYIYVIA TAPNMFNVND VLGVYSPHPY EQEVSALGGI PYSQIYGWYR
sp|P43530|ELAH_ECOLI        YSTYYIYVIA TAPNMFNVND VLGVYSPHPY EQEVSALGGI PYSQIYGWYR
tr|Q6U8A2|Q6U8A2_VIBCH      HSTYYIYVIA TAPNMFNVND VLGAYSPHPD EQEVSALGGI PYSQIYGWYR
tr|Q6U8A3|Q6U8A3_VIBCH      HSTYYIYVIA TAPNMFNVND VLGAYSPHPD EQGVSALGGI PYSQIYGWYR
sp|P43528|E2BA_ECOLI        YNEYYIYVVA AAPNLFDVNG VLGRYSPYPS ENEYAALGGI PLSQIIGWYR
sp|P13810|E2AA_ECOLI        YNEYYIYVVA PAPNLFDVNG VLGRYSPYPS ENEFAALGGI PLSQIIGWYR

sp|P01555|CHTA_VIBCH        VHFGVLDEQL HRNRGYRDRY YSNLDIAPAA DGYGLAGFPP EHRAWREEPW
tr|Q8L356|Q8L356_VIBCH      VHFGVLDEQL HRNRGYRDRY YSNLDIAPAA DGYGLAGFPP EHRAWREEPW
sp|P06717|ELAP_ECOLI        VNFGVIDERL HRNREYRDRY YRNLNIAPAE DGYRLAGFPP DHQAWREEPW
tr|O66280|O66280_ECOLI      VNFGVIDERL HRNREYRDRY YRNLNIAPAE DGYRLAGFPP DHQAWREEPW
sp|P43530|ELAH_ECOLI        VNFGVIDERL HRNREYRDRY YRNLNIAPAE DGYRLAGFPP DHQAWREEPW
tr|Q6U8A2|Q6U8A2_VIBCH      VHFGVLDEQL HRNRGYRDRY YSNLDIAPAA DGYGLAGFPP EHRAWREEPW
tr|Q6U8A3|Q6U8A3_VIBCH      VHFGVLDEQL HRNRGYRDRY YSNLDIAPAA DGYGLAGFPP EHRAWREEPW
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sp|P43528|E2BA_ECOLI        VSFGAIEGGM HRNRDYRRDL FRGLSAAPNE DGYRIAGFPD GFPAWEEVPW
sp|P13810|E2AA_ECOLI        VSFGAIEGGM QRNRDYRGDL FRGLTVAPNE DGYQLAGFPS NFPAWREMPW

sp|P01555|CHTA_VIBCH        IHHAPPGCGN APRSSMSNTC DEKTQSLGVK FLDEYQSKVK RQIFSGYQSD
tr|Q8L356|Q8L356_VIBCH      IHHAPPGCGN APRSSMSNTC DEKTQSLGVK FLDEYQSKVK RQIFSGYQSD
sp|P06717|ELAP_ECOLI        IHHAPQGCGN SSRTITGDTC NEETQNLSTI YLREYQSKVK RQIFSDYQSE
tr|O66280|O66280_ECOLI      IHHAPQGCGN SSRTITDDTC NEETQNLSTI YLRKYQSKVK RQIFSDYQSE
sp|P43530|ELAH_ECOLI        IHHAPQGCGN SSRTITGDTC NEETQNLSTI YLRKYQSKVK RQIFSDYQSE
tr|Q6U8A2|Q6U8A2_VIBCH      IHHAPPGCGN APRSS..... .......... .......... ..........
tr|Q6U8A3|Q6U8A3_VIBCH      IHHAPPGCGN APRSS..... .......... .......... ..........
sp|P43528|E2BA_ECOLI        REFAPNSCLP NNKASSDTTC ASLTNKLSQH DLADFKKYIK RKFTLMTLLS
sp|P13810|E2AA_ECOLI        STFAPEQCVP NNKEFKGGVC ISATNVLSKY DLMNFKKLLK RRLALTFFMS

sp|P01555|CHTA_VIBCH        ID.....THN RIKDEL
tr|Q8L356|Q8L356_VIBCH      ID.....THN RIEDEL
sp|P06717|ELAP_ECOLI        VD.....IYN RIRDEL
tr|O66280|O66280_ECOLI      VD.....IYN RIRDEL
sp|P43530|ELAH_ECOLI        VD.....IYN RIRNEL
tr|Q6U8A2|Q6U8A2_VIBCH      .......... ......
tr|Q6U8A3|Q6U8A3_VIBCH      .......... ......
sp|P43528|E2BA_ECOLI        INNDGFFSNN GGKDEL
sp|P13810|E2AA_ECOLI        E..DDFIGVH GERDEL
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UniProtKB/Swiss-Prot entry P01555

Note: most headings are clickable, even if they don't appear as links. They link to the user manual or other documents.

Entry information

Entry name	**CHTA_VIBCH**
Primary accession number	**P01555**
Secondary accession numbers	Q56634 Q9JPV1
Entered in Swiss-Prot in	Release 01, July 1986
Sequence was last modified in	Release 02, October 1986
Annotations were last modified in	Release 47, May 2005

Name and origin of the protein

Protein name	**Cholera enterotoxin, A chain [Precursor]**
Synonyms	**NAD(+)--diphthamide ADP-ribosyltransferase** **EC 2.4.2.36** **Cholera enterotoxin A subunit**
Contains	**Cholera enterotoxin subunit A1** (Cholera enterotoxin A1 chain) (Cholera enterotoxin alpha chain) **Cholera enterotoxin subunit A2** (Cholera enterotoxin A2 chain) (Cholera enterotoxin gamma chain)
Gene name	**Name: ctxA** Synonyms: toxA OrderedLocusNames: VC1457
From	Vibrio cholerae [TaxID: 666]
Taxonomy	Bacteria; Proteobacteria; Gammaproteobacteria; Vibrionales; Vibrionaceae; Vibrio.

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MEDLINE=84068199;PubMed=6646234 [NCBI, ExPASy, EBI, Israel, Japan]
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Comments

- ***FUNCTION***: The A1 chain catalyzes the ADP-ribosylation of Gs alpha, a GTP-binding regulatory protein, to activate the adenylate cyclase. This leads to an overproduction of cAMP and eventually to a hypersecretion of chloride and bicarbonate followed by water, resulting in the characteristic cholera stool. The A2 chain tethers A1 to the pentameric ring.
- ***CATALYTIC ACTIVITY***: NAD^+ + peptide diphthamide = nicotinamide + peptide N-(ADP-D-ribosyl)diphthamide.
- ***SUBUNIT***: The holotoxin (choleragen) consists of a pentameric ring of B subunits whose central pore is occupied by the A subunit. The A subunit contains two chains, A1 and A2, linked by a disulfide bridge.
- ***DOMAIN***: The four C-terminal residues of the A2 chain occupy the central pore of the holotoxin. Deletion of this residues weakens the interaction between the A subunit and the B pentamer whithout impairing the pentamer formation.
- ***MISCELLANEOUS***: After binding to gangliosides GM1 in lipid rafts, through the subunit B

pentamer, the holotoxin and the gangliosides are internalized. The holotoxin remains bound to GM1 until arrival in the ER. The A subunit has previously been cleaved in the intestinal lumen but the A1 and A2 chains have remained associated. In the ER, the A subunit disulfide bridge is reduced, the A1 chain is unfolded by the PDI and disassembled from the rest of the toxin. Then, the membrane-associated ER oxidase ERO1 oxidizes PDI, which releases the unfolded A1 chain. The next step is the retro-translocation of A1 into the cytosol. This might be mediated by the protein-conducting pore SEC61. Upon arrival in the cytosol, A1 refolds and avoids proteasome degradation. In one way or another, A1 finally reaches its target and induces toxicity.

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Cross-references

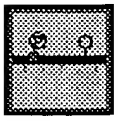
EMBL	X00171; CAA24995.1; -.	[EMBL / GenBank / DDBJ] [CoDingSequence]
	X58785; CAA41590.1; -.	[EMBL / GenBank / DDBJ] [CoDingSequence]
	D30053; BAA06290.1; -.	[EMBL / GenBank / DDBJ] [CoDingSequence]
	X58786; CAA41592.1; -.	[EMBL / GenBank / DDBJ] [CoDingSequence]
	K02679; AAA27514.1; -.	[EMBL / GenBank / DDBJ] [CoDingSequence]
	AF175708; AAD51359.1; -.	[EMBL / GenBank / DDBJ] [CoDingSequence]
	AE004224; AAF94614.1; -.	[EMBL / GenBank / DDBJ] [CoDingSequence]
	K01170; AAA27572.1; -.	[EMBL / GenBank / DDBJ] [CoDingSequence]
	D30052; BAA06288.1; -.	[EMBL / GenBank / DDBJ] [CoDingSequence]
PIR	A05129; XVVCA.	
PDB	1S5B; X-ray; A=19-258.	[ExPASy / RCSB / EBI]
	1S5C; X-ray; A=19-258.	[ExPASy / RCSB / EBI]
	1S5D; X-ray; A=19-258.	[ExPASy / RCSB / EBI]
	1S5E; X-ray; A/B=19-258.	[ExPASy / RCSB / EBI]
	1S5F; X-ray; A=19-258.	[ExPASy / RCSB / EBI]
	1XTC; X-ray; A=19-212, C=213-258.	[ExPASy / RCSB / EBI]
	Detailed list of linked structures.	
TIGR	VC1457; -.	
InterPro	IPR001144; Enterotoxin_A. Graphical view of domain structure.	
Pfam	PF01375; Enterotoxin_a; 1. Pfam graphical view of domain structure.	
PRINTS	PR00771; ENTEROTOXINA.	
ProDom	[Domain structure / List of seq. sharing at least 1 domain]	
HOGENOM	[Family / Alignment / Tree]	
BLOCKS	P01555.	
ProtoNet	P01555.	
ProtoMap	P01555.	
PRESAGE	P01555.	
DIP	P01555.	
ModBase	P01555.	
SWISS-2DPAGE	Get region on 2D PAGE.	
UniRef	View cluster of proteins with at least 50% / 90% identity.	

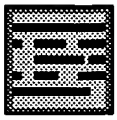
Keywords

3D-structure; **Complete proteome**; **Direct protein sequencing**; **Enterotoxin**; **Glycosyltransferase**;

NAD; Signal; Toxin; Transferase.

Features

 Feature table viewer

 Feature aligner

Key	From	To	Length	Description
SIGNAL	1	18	18	
CHAIN	19	212	194	Cholera enterotoxin subunit A1.
CHAIN	213	258	46	Cholera enterotoxin subunit A2.
ACT_SITE	130	130		*By similarity.*
BINDING	25	25		NAD *(By similarity)*.
BINDING	62	62		NAD *(By similarity)*.
DISULFID	205	217		Interchain (between A1 and A2 chains).
CONFLICT	20	20		D -> N (in Ref. 9).
CONFLICT	37	37		S -> R (in Ref. 10).
CONFLICT	39	39		G -> L (in Ref. 11).
CONFLICT	45	46		QS -> SE (in Ref. 11).
CONFLICT	111	111		N -> L (in Ref. 11).
CONFLICT	132	132		S -> A (in Ref. 11).
CONFLICT	213	213		M -> I (in Ref. 1).
CONFLICT	247	248		DI -> ID (in Ref. 12).
CONFLICT	256	256		D -> N (in Ref. 12).
STRAND	24	27	4	
HELIX	31	37	7	
TURN	38	38	1	
STRAND	39	40	2	
TURN	43	44	2	
TURN	48	49	2	
HELIX	59	63	5	
TURN	64	64	1	
TURN	75	76	2	
STRAND	77	81	5	
HELIX	85	89	5	
TURN	90	91	2	
TURN	96	97	2	
STRAND	101	106	6	
TURN	110	111	2	
STRAND	112	114	3	
HELIX	115	119	5	
HELIX	120	122	3	
HELIX	126	128	3	
STRAND	130	134	5	
STRAND	137	138	2	
TURN	139	141	3	
STRAND	142	148	7	
STRAND	153	159	7	
TURN	161	162	2	
HELIX	165	168	4	

TURN	169	170	2
HELIX	176	178	3
TURN	187	188	2
HELIX	190	193	4
TURN	195	196	2
HELIX	197	199	3
TURN	200	200	1
TURN	203	204	2
HELIX	215	251	37
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Sequence information

Length: **258 AA** [This is the length of the unprocessed precursor]

Molecular weight: **29336 Da** [This is the MW of the unprocessed precursor]

CRC64: **0F7EBAE62069A5D0** [This is a checksum on the sequence]

```
        10         20         30         40         50         60
MVKIIFVFFI FLSSFSYAND DKLYRADSRP PDEIKQSGGL MPRGQSEYFD RGTQMNINLY

        70         80         90        100        110        120
DHARGTQTGF VRHDDGYVST SISLRSAHLV GQTILSGHST YYIYVIATAP NMFNVNDVLG

       130        140        150        160        170        180
AYSPHPDEQE VSALGGIPYS QIYGWYRVHF GVLDEQLHRN RGYRDRYYSN LDIAPAADGY

       190        200        210        220        230        240
GLAGFPPEHR AWREEPWIHH APPGCGNAPR SSMSNTCDEK TQSLGVKFLD EYQSKVKRQI

       250
FSGYQSDIDT HNRIKDEL
```

P01555 in FASTA format

View entry in original Swiss-Prot format
View entry in raw text format (no links)
Report form for errors/updates in this Swiss-Prot entry

BLAST submission on ExPASy/SIB or at NCBI (USA)

Sequence analysis tools: ProtParam, ProtScale, Compute pI/Mw, PeptideMass, PeptideCutter, Dotlet (Java)

ScanProsite, MotifScan

Submit a homology modeling request to SWISS-MODEL

PileUp

MSF: 258 Type: P Check: 4420 ..

Name: sp|P01555|CHTA_VIBCH oo Len: 258 Check: 6104 Weight: 0.100
Name: sp|P43530|ELAH_ECOLI oo Len: 258 Check: 8316 Weight: 0.100

//

No leader sequence 19-212 29

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sp|P01555|CHTA_VIBCH      MVKIIFVFFI FLSSFSYAND DKLYRADSRP PDEIKQSGGL MPRGQSEYFD
sp|P43530|ELAH_ECOLI      MKNITFIFFI LLASPLYANG DKLYRADSRP PDEIKRSGGL MPRGHNEYFD

sp|P01555|CHTA_VIBCH      RGTQMNINLY DHARGTQTGF VRHDDGYVST SISLRSAHLV GQTILSGHST
sp|P43530|ELAH_ECOLI      RGTQMNINLY DHARGTQTGF VRYDDGYVST SLSLRSAHLA GQSILSGYST

sp|P01555|CHTA_VIBCH      YYIYVIATAP NMFNVNDVLG AYSPHPDEQE VSALGGIPYS QIYGWYRVHF
sp|P43530|ELAH_ECOLI      YYIYVIATAP NMFNVNDVLG VYSPHPYEQE VSALGGIPYS QIYGWYRVNF

sp|P01555|CHTA_VIBCH      GVLDEQLHRN RGYRDRYYSN LDIAPAADGY GLAGFPPEHR AWREEPWIHH
sp|P43530|ELAH_ECOLI      GVIDERLHRN REYRDRYYRN LNIAPAEDGY RLAGFPPDHQ AWREEPWIHH

sp|P01555|CHTA_VIBCH      APPGCGNAPR SSMSNTCDEK TQSLGVKFLD EYQSKVKRQI FSGYQSDIDT
sp|P43530|ELAH_ECOLI      APQGCGNSSR TITGDTCNEE TQNLSTIYLR KYQSKVKRQI FSDYQSEVDI

sp|P01555|CHTA_VIBCH      HNRIKDEL
sp|P43530|ELAH_ECOLI      YNRIRNEL
```

CLUSTAL W (1.74) multiple sequence alignment

```
sp|P01555|CHTA_VIBCH      MVKIIFVFFIFLSSFSYANDDKLYRADSRPPDEIKQSGGLMPRGQSEYFDRGTQMNIN
sp|P43530|ELAH_ECOLI      MKNITFIFFILLASPLYANGDKLYRADSRPPDEIKRSGGLMPRGHNEYFDRGTQMNIN
                          * :* *:***:*:*  ***.***************:********:.***********

sp|P01555|CHTA_VIBCH      DHARGTQTGFVRHDDGYVSTSISLRSAHLVGQTILSGHSTYYIYVIATAPNMFNVNDV
sp|P43530|ELAH_ECOLI      DHARGTQTGFVRYDDGYVSTSLSLRSAHLAGQSILSGYSTYYIYVIATAPNMFNVNDV
                          ************:********:*******.**:****:********************

sp|P01555|CHTA_VIBCH      AYSPHPDEQEVSALGGIPYSQIYGWYRVHFGVLDEQLHRNRGYRDRYYSNLDIAPAAD
sp|P43530|ELAH_ECOLI      VYSPHPYEQEVSALGGIPYSQIYGWYRVNFGVIDERLHRNREYRDRYYRNLNIAPAED
                          .***** **********************:***:**:***** ****** **:**** *

sp|P01555|CHTA_VIBCH      GLAGFPPEHRAWREEPWIHHAPPGCGNAPRSSMSNTCDEKTQSLGVKFLDEYQSKVKR
sp|P43530|ELAH_ECOLI      RLAGFPPDHQAWREEPWIHHAPQGCGNSSRTITGDTCNEETQNLSTIYLRKYQSKVKR
                           ******:*:************ ****:.*:  .:**:*:**.*.. :* :*******

sp|P01555|CHTA_VIBCH      FSGYQSDIDTHNRIKDEL
sp|P43530|ELAH_ECOLI      FSDYQSEVDIYNRIRNEL
                          **.***::* :***::**
```

```
CLUSTAL W (1.74) multiple sequence alignment


tr|Q77DI6|Q77DI6_9VIRU      MVKIIFVFFIFLSSFSYANDDKLYRADSRPPDEIKQSGGLMPRGQSEYFD
tr|O66280|O66280_ECOLI      MKNITFIFFILLASPLYANGDKLYRADSRPPDEIKRSGGLMPRGHNEYFD
                            * :* *:***:*:*  ***.***************:********:.****

tr|Q77DI6|Q77DI6_9VIRU      RGTQMNINLYDHARGTQTGFVRHDDGYVSTSISLRSAHLVGQTILSGHST
tr|O66280|O66280_ECOLI      RGTQMNINLYDHARGTQTGFVRYDDGYVSTSLSLRSAHLAGQSILSGYST
                            **********************:********:*******.**:****:**

tr|Q77DI6|Q77DI6_9VIRU      YYIYVIATAPNMFNVNDVLGAYSPHPDEQEVSALGGIPYSQIYGWYRVHF
tr|O66280|O66280_ECOLI      YYIYVIATAPNMFNVNDVLGVYSPHPYEQEVSALGGIPYSQIYGWYRVNF
                            ********************.***** **********************:*

tr|Q77DI6|Q77DI6_9VIRU      GVLDEQLHRNRGYRDRYYSNLDIAPAADGYGLAGFPPEHRAWREEPWIHH
tr|O66280|O66280_ECOLI      GVIDERLHRNREYRDRYYRNLNIAPAEDGYRLAGFPPDHQAWREEPWIHH
                            **:**:***** ****** **:**** *** ******:*:**********

tr|Q77DI6|Q77DI6_9VIRU      APPGCGNAPRSSMSNTCDEKTQSLGVKFLDEYQSKVKRQIFSGYQSDIDT
tr|O66280|O66280_ECOLI      APQGCGNSSRTITDDTCNEETQNLSTIYLRKYQSKVKRQIFSDYQSEVDI
                            ** ****:.*:  .:**:*:**.*.. :* :***********.***::*

tr|Q77DI6|Q77DI6_9VIRU      HNRIKDEL
tr|O66280|O66280_ECOLI      YNRIRDEL
                            :***:***
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PileUp

MSF: 258 Type: P Check: 4011 ..

Name: tr|Q77DI6|Q77DI6_9VIRU oo Len: 258 Check: 6104 Weight: 0.100
Name: tr|O66280|O66280_ECOLI oo Len: 258 Check: 7907 Weight: 0.100

//

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tr|Q77DI6|Q77DI6_9VIRU      MVKIIFVFFI FLSSFSYAND DKLYRADSRP PDEIKQSGGL MPRGQSEYFD
tr|O66280|O66280_ECOLI      MKNITFIFFI LLASPLYANG DKLYRADSRP PDEIKRSGGL MPRGHNEYFD

tr|Q77DI6|Q77DI6_9VIRU      RGTQMNINLY DHARGTQTGF VRHDDGYVST SISLRSAHLV GQTILSGHST
tr|O66280|O66280_ECOLI      RGTQMNINLY DHARGTQTGF VRYDDGYVST SLSLRSAHLA GQSILSGYST

tr|Q77DI6|Q77DI6_9VIRU      YYIYVIATAP NMFNVNDVLG AYSPHPDEQE VSALGGIPYS QIYGWYRVHF
tr|O66280|O66280_ECOLI      YYIYVIATAP NMFNVNDVLG VYSPHPYEQE VSALGGIPYS QIYGWYRVNF

tr|Q77DI6|Q77DI6_9VIRU      GVLDEQLHRN RGYRDRYYSN LDIAPAADGY GLAGFPPEHR AWREEPWIHH
tr|O66280|O66280_ECOLI      GVIDERLHRN REYRDRYYRN LNIAPAEDGY RLAGFPPDHQ AWREEPWIHH

tr|Q77DI6|Q77DI6_9VIRU      APPGCGNAPR SSMSNTCDEK TQSLGVKFLD EYQSKVKRQI FSGYQSDIDT
tr|O66280|O66280_ECOLI      APQGCGNSSR TITDDTCNEE TQNLSTIYLR KYQSKVKRQI FSDYQSEVDI

tr|Q77DI6|Q77DI6_9VIRU      HNRIKDEL
tr|O66280|O66280_ECOLI      YNRIRDEL
```

sp P06717 ELAP_ECOLI **Heat-labile enterotoxin A chain precursor (LT-A, porcine) (LTP-A) [eltA] [Escherichia coli]** 258 AA align

Score = 427 bits (1099), Expect = e-119
Identities = 198/242 (81%), Positives = 222/242 (90%)

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Query: 17  YANDDKLYRADSRPPDEIKQSGGLMPRGQSEYFDRGTQMNINLYDHARGTQTGFVRHDDG 76
           YAN D+LYRADSRPPDEIK+SGGLMPRG +EYFDRGTQMNINLYDHARGTQTGFVR+DDG
Sbjct: 17  YANGDRLYRADSRPPDEIKRSGGLMPRGHNEYFDRGTQMNINLYDHARGTQTGFVRYDDG 76

Query: 77  YVSTSISLRSAHLVGQTILSGHSTYYIYVIATAPNMFNVNDVLGAYSPHPDEQEVSALGG 136
           YVSTS+SLRSAHL GQ+ILSG+STYYIYVIATAPNMFNVNDVLG YSPHP EQEVSALGG
Sbjct: 77  YVSTSLSLRSAHLAGQSILSGYSTYYIYVIATAPNMFNVNDVLGVYSPHPYEQEVSALGG 136

Query: 137 IPYSQIYGWYRVHFGVLDEQLHRNRGYRDRYYSNLDIAPAADGYGLAGFPPEHRAWREEP 196
           IPYSQIYGWYRV+FGV+DE+LHRNR YRDRYY NL+IAPA DGY LAGFPP+H+AWREEP
Sbjct: 137 IPYSQIYGWYRVNFGVIDERLHRNREYRDRYYRNLNIAPAEDGYRLAGFPPDHQAWREEP 196

Query: 197 WIHHAPPGCGNAPRSSMSNTCDEKTQSLGVKFLDEYQSKVKRQIFSGYQSDIDTHNRIKD 256
           WIHHAP GCGN+ R+   +TC+E+TQ+L   +L EYQSKVKRQIFS YQS++D +NRI+D
Sbjct: 197 WIHHAPQGCGNSSRTITGDTCNEETQNLSTIYLREYQSKVKRQIFSDYQSEVDIYNRIRD 256

Query: 257 EL 258
           EL
Sbjct: 257 EL 258
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CLUSTAL FORMAT for T-COFFEE Version_1.37, CPU=0.13 sec, SCORE=11330, Nseq=2, Len=258

unk|VIRT70|Blast_submission  MVKIIFVFFIFLSSFSYANDDKLYRADSRPPDEIKQSGGLMPRGQSEYFDRGTQM
sp|P06717|ELAP_ECOLI         MKNITFIFFILLASPLYANGDRLYRADSRPPDEIKRSGGLMPRGHNEYFDRGTQM
                             * :* *:***:*:*  ***.*:*************:********:.*********

unk|VIRT70|Blast_submission  DHARGTQTGFVRHDDGYVSTSISLRSAHLVGQTILSGHSTYYIYVIATAPNMFNV
sp|P06717|ELAP_ECOLI         DHARGTQTGFVRYDDGYVSTSLSLRSAHLAGQSILSGYSTYYIYVIATAPNMFNV
                             ************:********:*******.**:****:*****************

unk|VIRT70|Blast_submission  AYSPHPDEQEVSALGGIPYSQIYGWYRVHFGVLDEQLHRNRGYRDRYYSNLDIAP
sp|P06717|ELAP_ECOLI         VYSPHPYEQEVSALGGIPYSQIYGWYRVNFGVIDERLHRNREYRDRYYRNLNIAP
                             .***** **********************:***:**:***** ****** **:***

unk|VIRT70|Blast_submission  GLAGFPPEHRAWREEPWIHHAPPGCGNAPRSSMSNTCDEKTQSLGVKFLDEYQSK
sp|P06717|ELAP_ECOLI         RLAGFPPDHQAWREEPWIHHAPQGCGNSSRTITGDTCNEETQNLSTIYLREYQSK
                              ******:*:************ ****:.*:  .:**:*:**.*.. :* *****

unk|VIRT70|Blast_submission  FSGYQSDIDTHNRIKDEL
sp|P06717|ELAP_ECOLI         FSDYQSEVDIYNRIRDEL
                             **.***::* :***:***
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UniProtKB/Swiss-Prot entry P06717

Note: most headings are clickable, even if they don't appear as links. They link to the user manual or other documents.

Entry information

Entry name	**ELAP_ECOLI**
Primary accession number	**P06717**
Secondary accession number	P01554
Entered in Swiss-Prot in	Release 06, January 1988
Sequence was last modified in	Release 06, January 1988
Annotations were last modified in	Release 47, May 2005

Name and origin of the protein

Protein name	**Heat-labile enterotoxin A chain [Precursor]**
Synonyms	**LT-A, porcine** **LTP-A**
Gene name	**Name: eltA** Synonyms: ltpA
From	Escherichia coli [TaxID: 562]
Taxonomy	Bacteria; Proteobacteria; Gammaproteobacteria; Enterobacteriales; Enterobacteriaceae; Escherichia.

References

[1] NUCLEOTIDE SEQUENCE.
STRAIN=Isolate P307 / ETEC, and Isolate PCG86 / ETEC;
MEDLINE=87137303;PubMed=3546273 [NCBI, ExPASy, EBI, Israel, Japan]
Yamamoto T., Gojobori T., Yokota T.;
"Evolutionary origin of pathogenic determinants in enterotoxigenic Escherichia coli and Vibrio cholerae O1.";
J. Bacteriol. 169:1352-1357(1987).

[2] NUCLEOTIDE SEQUENCE.
STRAIN=Isolate P307 / ETEC;
Dykes C.W., Halliday I.J., Hobden A.N., Read M.J., Harford S.;
"A comparison of the nucleotide sequence of the A subunit of heat-labile enterotoxin and cholera toxin.";
FEMS Microbiol. Lett. 26:171-174(1985).

[3] NUCLEOTIDE SEQUENCE.
STRAIN=Isolate P307 / ETEC;
MEDLINE=82167425;PubMed=6279611 [NCBI, ExPASy, EBI, Israel, Japan]
Spicer E.K., Noble J.A.;
"Escherichia coli heat-labile enterotoxin. Nucleotide sequence of the A subunit gene.";
J. Biol. Chem. 257:5716-5721(1982).

[4] NUCLEOTIDE SEQUENCE OF 19-258.
STRAIN=Isolate P307 / ETEC;
MEDLINE=91093102;PubMed=2266142 [NCBI, ExPASy, EBI, Israel, Japan]
Tsuji T., Inoue T., Miyama A., Okamoto K., Honda T., Miwatani T.;
"A single amino acid substitution in the A subunit of Escherichia coli enterotoxin results in a loss of its toxic activity.";
J. Biol. Chem. 265:22520-22525(1990).

[5] NUCLEOTIDE SEQUENCE OF 1-40.
Trachman J.D., Maas W.K.;
Submitted (JUL-1991) to the EMBL/GenBank/DDBJ databases.

[6] X-RAY CRYSTALLOGRAPHY (2.3 ANGSTROMS).
DOI=10.1038/351371a0;MEDLINE=91238966;PubMed=2034287 [NCBI, ExPASy, EBI, Israel, Japan]
Sixma T.K., Pronk S.E., Kalk K.H., Wartna E.S., van Zanten B.A.M., Witholt B., Hol W.G.J.;
"Crystal structure of a cholera toxin-related heat-labile enterotoxin from E. coli.";
Nature 351:371-377(1991).

[7] X-RAY CRYSTALLOGRAPHY (1.95 ANGSTROMS).
MEDLINE=93240541;PubMed=8478941 [NCBI, ExPASy, EBI, Israel, Japan]
Sixma T.K., van Zanten B.A.M., Dauter Z., Hol W.G.J.;
"Refined structure of Escherichia coli heat-labile enterotoxin, a close relative of cholera toxin.";
J. Mol. Biol. 230:890-918(1993).

[8] X-RAY CRYSTALLOGRAPHY (2.4 ANGSTROMS) OF 19-258, AND MUTAGENESIS OF ARG-25; VAL-71; ARG-72; TYR-77; SER-81; ALA-90; VAL-115; TYR-122; HIS-125; GLU-128; GLU-130; SER-132 AND ARG-210.
PubMed=7830560 [NCBI, ExPASy, EBI, Israel, Japan]
Pizza M., Domenighini M., Hol W., Giannelli V., Fontana M.R., Giuliani M.M., Magagnoli C., Peppoloni S., Manetti R., Rappuoli R.;
"Probing the structure-activity relationship of Escherichia coli LT-A by site-directed mutagenesis.";
Mol. Microbiol. 14:51-60(1994).

[9] DISCUSSION OF SEQUENCE.
MEDLINE=95349400;PubMed=7623669 [NCBI, ExPASy, EBI, Israel, Japan]
Domenighini M., Pizza M., Jobling M.G., Holmes R.K., Rappuoli R.;
"Identification of errors among database sequence entries and comparison of correct amino acid sequences for the heat-labile enterotoxins of Escherichia coli and Vibrio cholerae.";
Mol. Microbiol. 15:1165-1167(1995).

Comments

- ***FUNCTION***: The biological activity of the toxin is produced by the A chain, which activates intracellular adenyl cyclase.
- ***SUBUNIT***: Heterohexamer of one A chain and of five B chains.

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Cross-references

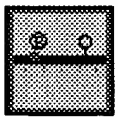
EMBL	M15361; AAA24791.1; -.[EMBL / GenBank / DDBJ] [CoDingSequence] M15362; AAA24793.1; -.[EMBL / GenBank / DDBJ] [CoDingSequence] M35581; AAA98202.1; -.[EMBL / GenBank / DDBJ] [CoDingSequence] V00275; CAA23532.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence] M57244; AAB59161.1; -.[EMBL / GenBank / DDBJ] [CoDingSequence]

	M61015; AAA24335.1; -.[EMBL / GenBank / DDBJ] [CoDingSequence] A04913; CAA00402.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
PIR	I55231; QLECA.
PDB	1HTL; X-ray; A=19-209, C=210-258.[ExPASy / RCSB / EBI] 1LT3; X-ray; A=19-258. [ExPASy / RCSB / EBI] 1LT4; X-ray; A=19-258. [ExPASy / RCSB / EBI] 1LTA; X-ray; A=19-206, C=210-258.[ExPASy / RCSB / EBI] 1LTB; X-ray; A=22-206, C=210-254.[ExPASy / RCSB / EBI] 1LTG; X-ray; A=19-209, C=210-258.[ExPASy / RCSB / EBI] 1LTI; X-ray; A=19-210, C=211-258. [ExPASy / RCSB / EBI] 1LTS; X-ray; A=22-206, C=214-254. [ExPASy / RCSB / EBI] 1LTT; X-ray; A=22-206, C=214-254.[ExPASy / RCSB / EBI] Detailed list of linked structures.
InterPro	IPR001144; Enterotoxin_A. Graphical view of domain structure.
Pfam	PF01375; Enterotoxin_a; 1. Pfam graphical view of domain structure.
PRINTS	PR00771; ENTEROTOXINA.
ProDom	[Domain structure / List of seq. sharing at least 1 domain]
HOGENOM	[Family / Alignment / Tree]
BLOCKS	P06717.
ProtoNet	P06717.
ProtoMap	P06717.
PRESAGE	P06717.
DIP	P06717.
ModBase	P06717.
SWISS-2DPAGE	Get region on 2D PAGE.
UniRef	View cluster of proteins with at least 50% / 90% identity.

Keywords

3D-structure; **Enterotoxin**; **Signal**; **Toxin**.

Features


Feature table viewer

Key	From	To	Length	Description
SIGNAL	1	18	18	
CHAIN	19	258	240	Heat-labile enterotoxin A chain.
ACT_SITE	130	130		
NP_BIND	25	39	15	NAD.
DISULFID	205	217		
VARIANT	130	130	1	E -> K (in inactive mutant).
MUTAGEN	25	25		R->K: Abolishes toxicity.
MUTAGEN	71	71		V->D,E: Abolishes toxicity.
MUTAGEN	72	72		R->A,K: No effect.
MUTAGEN	77	77		Y->M: No effect.
MUTAGEN	81	81		S->K: Abolishes toxicity.

MUTAGEN	90	90	A->E,H,R: No effect.
MUTAGEN	115	115	V->K: Abolishes toxicity.
MUTAGEN	122	122	Y->D,K: Abolishes toxicity.
MUTAGEN	125	125	H->E: Strongly reduces toxicity.
MUTAGEN	128	128	E->S: Abolishes toxicity.
MUTAGEN	130	130	E->S: Abolishes toxicity.
MUTAGEN	132	132	S->E,K: Abolishes toxicity.
MUTAGEN	210	210	R->N: No effect.
CONFLICT	37	39	SGG -> FRS (in Ref. 3).
CONFLICT	45	45	Missing (in Ref. 3).
CONFLICT	93	93	S -> Y (in Ref. 3).
CONFLICT	100	110	TYYIYVIATAP -> LTIYIVIA (in Ref. 3).
CONFLICT	119	120	LG -> IS (in Ref. 3).
CONFLICT	159	159	R -> G (in Ref. 4).
CONFLICT	207	207	N -> D (in Ref. 3).
STRAND	23	27	5
HELIX	31	37	7
TURN	38	38	1
STRAND	39	40	2
TURN	43	44	2
TURN	48	49	2
TURN	51	52	2
HELIX	59	64	6
STRAND	67	67	1
TURN	68	69	2
STRAND	70	70	1
STRAND	77	81	5
HELIX	84	94	11
TURN	96	97	2
STRAND	100	106	7
TURN	110	111	2
STRAND	112	114	3
HELIX	115	119	5
HELIX	120	122	3
TURN	127	128	2
STRAND	130	134	5
TURN	135	135	1
STRAND	137	138	2
HELIX	139	141	3
STRAND	142	149	8
TURN	150	151	2
STRAND	152	159	8
TURN	161	162	2
HELIX	165	168	4
TURN	169	170	2
STRAND	174	174	1
HELIX	176	178	3
TURN	179	179	1

HELIX	180	182	3
TURN	187	188	2
HELIX	190	193	4
TURN	195	196	2
HELIX	197	200	4
TURN	203	204	2
HELIX	215	240	26
HELIX	241	244	4
HELIX	250	253	4

Sequence information

Length: **258 AA** [This is the length of the unprocessed precursor]

Molecular weight: **29902 Da** [This is the MW of the unprocessed precursor]

CRC64: **2F0786442619F81F** [This is a checksum on the sequence]

```
        10         20         30         40         50         60
MKNITFIFFI LLASPLYANG DRLYRADSRP PDEIKRSGGL MPRGHNEYFD RGTQMNINLY

        70         80         90        100        110        120
DHARGTQTGF VRYDDGYVST SLSLRSAHLA GQSILSGYST YYIYVIATAP NMFNVNDVLG

       130        140        150        160        170        180
VYSPHPYEQE VSALGGIPYS QIYGWYRVNF GVIDERLHRN REYRDRYYRN LNIAPAEDGY

       190        200        210        220        230        240
RLAGFPPDHQ AWREEPWIHH APQGCGNSSR TITGDTCNEE TQNLSTIYLR EYQSKVKRQI

       250
FSDYQSEVDI YNRIRDEL
```

P06717 in FASTA format

View entry in original Swiss-Prot format
View entry in raw text format (no links)
Report form for errors/updates in this Swiss-Prot entry

BLAST submission on ExPASy/SIB or at NCBI (USA)

Sequence analysis tools: ProtParam, ProtScale, Compute pI/Mw, PeptideMass, PeptideCutter, Dotlet (Java)

ScanProsite, MotifScan

Submit a homology modeling request to SWISS-MODEL

[0038] Other suitable CT-CRM proteins may include those in which one or more of the amino acid residues includes a substituted group. Still another suitable CT-CRM holotoxin protein is one in which the CT-CRM polypeptide is fused with another compound, such as a compound to increase the half-life of the polypeptide (for example, polyethylene glycol). Another suitable CT-CRM protein is one in which additional amino acids are fused to the polypeptide, such as a leader or secretory sequence, or a sequence which is employed to enhance the immunogenicity of the CT-CRM protein. Still other modifications of the CT-CRMs include the above-mentioned deletion of the CT-A signal or leader sequence at the N terminus of CT, i.e., amino acids 1-18 of SEQ ID NO: 1 and/or the deletion of the CT-B signal or leader sequence at amino acids 259-279 of SEQ ID NO: 1, and/or the deletion of other regions that do not effect immunogenicity. Similarly, a modification of the CT-CRMs described herein includes include replacing either signal or leader sequence with another signal or leader sequence. See, e.g., U.S. Pat. No. 5,780,601, incorporated by reference herein.

CT-CRM

[0063] The terms "substantial homology" or "substantial similarity," when referring to a nucleic acid or fragment thereof, indicates that, when optimally aligned with appropriate nucleotide insertions or deletions with another nucleic acid (or its complementary strand), there is nucleotide sequence identity in at least about 70% of the nucleotide bases, as measured by any well-known algorithm of sequence identity, such as FASTA, a program in GCG Version 6.1. The term "homologous" as used herein, refers to the sequence similarity between two polymeric molecules, e.g., between two nucleic acid molecules, e.g., two DNA molecules or two RNA molecules, or between two polypeptide molecules. When a nucleotide or amino acid position in both of the two molecules is occupied by the same monomeric nucleotide or amino acid, e.g., if a position in each of two DNA molecules is occupied by adenine, then they are homologous at that position. The homology between two sequences is a direct function of the number of matching or homologous positions, e.g. if half (e.g., five positions in a polymer ten subunits in length) of the positions in two compound sequences are homologous then the two sequences are 50% hormologous. If 90% of the positions, e.g., 9 of 10, are matched or homologous, the two sequences share 90% homology. By way of example, the DNA sequences 3'ATTGCC5' and 3'TATGCG5' share 50% homology. By the term "substantially homologous" as used herein, is meant DNA or RNA which is about 70% homologous, more preferably about 80% homologous and most preferably about 90% homologous to the desired nucleic acid.